# IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| Applicant(s): Spriggs, et al. | |
| Application No.: 10/595,135 | Group Art Unit: 1643 |
| Filed: 3/2/2006 | |
| Title: Method for Early Detection of Ovarian Cancer | Examiner: Hong Sang |
| | Confirmation No: 3258 |
| Attorney Docket No.: MSK.P-071 | |
| Customer No.: 057381 | |

Commissioner for Patents

PO Box 1450

Alexandria, VA 22313-1450

## AMENDMENT

Dear Sir:

This is in response to the Office Action mailed June 8, 2009 for the above-captioned application. Reconsideration and further examination are respectfully requested.

Claims 1-14 are pending in this application.

Claims 1, 2, 9 and 11-14 stand rejected under 35 USC § 102(b) as being anticipated by WO 00/19206. In order for this rejection to be proper, the cited reference must disclose each and every element of the claimed invention. In the present case, independent claim 1 recites:

> 1.      A method for detection of ovarian cancer in an individual who has not been diagnosed with ovarian cancer and who is not displaying symptoms associated with stage III or IV ovarian cancer, comprising the steps of
> (a)      obtaining a sample from the individual;
> (b)      determining the amount of expressed YKL-40 in the sample; and
> (c)      comparing the amount of expressed YKL-40 determined to a pre-determined threshold, wherein if the predetermined threshold is exceeded, the test is deemed to be an indicator of ovarian cancer in the individual.

This claim is directed to ovarian cancer specifically. The cited reference is not specific to any cancer, but as summarized by the examiner supposedly relates to cancer generally. Moreover, the results on Page 59, Table 6 that show that two of the 197 patients in the study ultimately developed ovarian cancer do not teach the present method even indirectly because one of these two patients had an elevated YKL-40 level and the other did not.

It is noted from consideration of the § 103 rejection that the Examiner apparently assumes that these levels (198 µg/L and 298 µ/L) are both elevated based on a misunderstanding of the teaching of the reference. Page 28 refers to two methods for determining a difference of sufficient significance to be considered a positive result. In the one referred to by the examiner, the standard is "greater than the 95% of controls." This is not artfully stated, but anyone taking into account the previous paragraph and a basic understanding of statistics, one skilled in the art would understand that this means that to be statistically different, a measured value needs to be greater than 95% of the control values measured. It is further noted that

> If a data distribution is approximately normal then about 68% of the values are within 1 standard deviation of the mean (mathematically, $\mu \pm s$, where $\mu$ is the arithmetic mean), about 95% of the values are within two standard deviations ($\mu \pm 2s$), and about 99.7% lie within 3 standard deviations ($\mu \pm 3s$). This is known as the 68-95-99.7 rule, or the empirical rule.

http://en.wikipedia.org/wiki/Standard_deviation. Thus, the reference to 95% appears to bear some relationship to this common value in statistics.

It should be understood that this standard bears no relationship to a "level greater than 95% of the median level" which the Examiner states is taught by the reference. A sample can not be considered significantly higher than a control when it is below the median (or the mean) value of the control samples, which this standard would permit. Furthermore, Page 46 which states that median level of the control group was 99 µg/L also states that the 95% level was 207 µg/L, consistent with the value on Page 28. This comparison with the actual numbers in Table 6 shows that one is below the level and one is above. The same result obtains when the statistical threshold referenced in the table (247 µg/L) is used. Furthermore, there is no teaching that there was early stage ovarian cancer present in either the women who presented with ovarian cancer at some undisclosed time in the next five years. Thus, there is no teaching in the reference that provides the person skilled in the art that provides any reason to conclude that YKL-40 is an indicator useful for early detection of ovarian cancer as presently claimed.

For these reasons, Applicants submit that the claims of this application are not anticipated by the cited reference. The rejection should therefore be withdrawn.

Appln No.: 10/595,135
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Reply to Office Action of June 8, 2009

Claims 1-14 are rejected under 35 USC § 103 as obvious over WO 00/19206 as discussed above in view of Marton and Xu et al. These claims recite the specific threshold of two standard deviations above the mean. As discussed above, Applicant agree with the Examiner's contention that this threshold is a statistical commonplace, and indeed have pointed out that the reference uses a very similar threshold. The problem remains, however, that the reference provides no showing of a statistical relationship between serum YKL-40 levels and later onset of ovarian cancer, and certainly provides no suggestion of statistical significance of a relationship between early stage ovarian cancer and a concurrent measurement of elevated YKL-40 levels. Thus, there is no teaching, and no suggestion of the invention.

For these reasons, this application is now considered to be in condition for allowance and such action is earnestly solicited.

Respectfully submitted,

Marina T. Larson, Ph.D
Attorney/Agent for Applicant(s)
Reg. No. 32038

(970) 262-1800